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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,335	08/15/2001	Graham Paul Matthews	4-30811A/C1	1679

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 10/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,335	MATTHEWS ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weder et al. (US 5726164) in view of Fricker et al. (US 5932243), and if necessary, further in view of Goldstein et al. (US 5599808), Caravatti et al. (US 5093330) and/or Henry et al. (US 5736542).

This rejection is analogous to the original rejection.

Response to Arguments

Applicant's arguments filed June 26, 2003 have been fully considered but they are not persuasive.

Applicants argument takes position that the active ingredient in Fricker's 243, rapamycin, differs from the active ingredient N-benzoyl-staurosporine by chemical structures and the differences in these two types of chemical structures would not lead one of the skilled in the art to predict that the particular solubility problems could be overcome with the combined teachings of Weder' 164, Fricker'243, Caravatti'330, Goldstein'808 and Henry'542. Furthermore, the applicants argues that the physical changes in formulation components, based on the chemical differences of the molecules, is inherently seen by the fact that additional stabilizers are useful in the present invention and that a higher dosage of active ingredient may be used than in the formulation of Fricker'243.

Although the examiner agrees with applicants in regards to the structural difference between the active ingredient, rapamycin, in Fricker's 243 and the active ingredient in the instant invention, N-benzoyl-staurosporine, the examiner maintains that the preparation of the claimed composition would have been apparent to those skilled in the art. It is noted to applicant that the examiner's reference to Fricker'324, Goldstein'808, Caravatti'330 and Henry'542 is to show the relative skill of the prior art. As evidenced by Fricker'243, Caravatti'330, Goldstein'808 and Henry'542, all the secondary ingredients employed (i.e., hydrophilic component, lipophilic component and surfactants) herein are known to be useful as formulation base that is suitable for

intravenous dosage forms and oral dosage forms. This is also recognized in Weder'164 in column 6, lines 52-62: "That formulation base is suitable both for intravenous dosage forms and for those dosage forms in which the solubilisation of a sparingly soluble active ingredient is necessary, for example capsule fillings, drops, lotions or emulsions for ointments, gels, creams etc. To the latter there may also be added the other excipients typical of such dosage forms. The formulation base can be used both for solubilising sparingly soluble staurosporin derivatives in accordance with the stated object of this invention and for solubilising other sparingly soluble active ingredients". In examiner's opinion, the claimed N-benzoyl-staurosporine formulation would have been apparent to those skilled in the art, absent showing superior unexpected results over the prior art. Applicants mere statement of "surprising success shown in the present invention" cannot be considered as an overcoming evidence for this 35 USC 103 obviousness rejection. In addition, optimization of amounts of known active and inactive ingredients in a composition is well considered within the skill of the artisan.

Applicant's argument takes position that the instantly claimed bioavailability determination of N-benzoyl-staurosporine (claim 11) cannot be predicted because such bioavailability results are well known to be specific to a drug, compositions, and inactive component type and quantity used in such compositions.

The examiner disagrees. Unlike applicants argument, determinations of trough level, Cmax and AUC of the drug are routinely performed by medical professionals (e.g., physician and pharmacist) to deliver optimum therapeutic effect of the drug without undue experimentation in clinical setting. Further refinement of the calculations necessary to deliver optimum

therapeutic effect of the drug are routinely made by those ordinary skill in the art as determined by good medical practice and the clinical condition of the individual patient.

Applicant's argument takes position that the characteristic of the instant N-benzoyl-staurosporine bieng spontaneously dispersible into nanometer sized particles in an aqueous environment is not taught or suggested by any of the references cited by the examiner.

The examiner disagrees. Unlike applicants argument, the formulation of N-benzoylstaurosporine in "nanosuspension" is well recognized in Weder'164. Weder'164 in column 3, lines 25-29 states: "Electron microscope images show that a population of more than 95% of the sparingly soluble active ingredient is present in the form of a suspension of particles having a particle size of approximately 5-20 nm". As stated above, the instant claim invention differs mainly from the teaching of Weder'164 in the different dosage formulation, namely oral composition and the specific dosage amount of active and inactive ingredients to provide optimum bioavilability of the drug. However, such determination of optimum dosage form or optimum dosage amounts would have been apparent to those skilled in the art, absent showing superior unexpected results over the prior art.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600